

CLAIMS

37. A bispecific antibody comprising:
 - a) a first antibody binding specificity which confers the ability of the bispecific antibody to cross the blood-brain barrier; and
 - b) a second antibody specificity conferring the ability of the bispecific antibody to bind to a β -amyloid epitope.
38. The bispecific antibody of Claim 37 which is produced by fusing a first and a second hybridoma clone, the first hybridoma clone generating the specificity of step a) and the second hybridoma clone generating the specificity of step b).
39. The bispecific antibody of Claim 37 which is produced by recombinant DNA techniques.
40. The bispecific antibody of Claim 37 wherein the first and second antibody binding specificities are provided by chemically linking a first antibody, or fragment thereof, to a second antibody, or fragment thereof.
41. The bispecific antibody of Claim 40 wherein the first and second antibodies are monoclonal antibodies.
42. The bispecific antibody of Claim 40 which is an F(ab')₂ hybrid.
43. The bispecific antibody of Claim 39 which is a single chain Fv heterobispecific dimer.

44. The bispecific antibody of Claim 37 wherein the second antibody specificity further confers the ability of the bispecific antibody to inhibit the formation of β -amyloid plaques.
45. The bispecific antibody of Claim 37 wherein the second antibody specificity further confers the ability of the bispecific antibody to disaggregate preformed β -amyloid plaques.
46. The bispecific antibody of Claim 37 wherein the second antibody specificity is further characterized by the ability to hydrolytically cleave β -amyloid.
47. A method for inhibiting the formation of β -amyloid plaques in the brain of a human, the method comprising:
 - a) providing a bispecific antibody comprising:
 - i) a first antibody binding specificity which confers the ability of the bispecific antibody to cross the blood-brain barrier; and
 - ii) a second antibody specificity conferring the ability of the bispecific antibody to bind to a β -amyloid epitope; and
 - b) introducing the bispecific antibody of step a) into the circulatory system of the human at a concentration sufficient to result in transcytosis of the bispecific antibody across the blood brain barrier.

48. The method of Claim 47 wherein the bispecific antibody is produced by fusing a first and a second hybridoma clone, the first hybridoma clone generating the specificity of step a) i) and the second hybridoma clone generating the specificity of step a) ii).
49. The method of Claim 47 wherein the bispecific antibody is produced by recombinant DNA techniques.
50. The method of Claim 47 wherein the first and second antibody binding specificities are provided by chemically linking a first antibody, or fragment thereof, to a second antibody, or fragment thereof.
51. The method of Claim 50 wherein the first and second antibodies are monoclonal antibodies.
52. The method of Claim 50 wherein the bispecific antibody is an F(ab')₂ hybrid.
53. The method of Claim 49 wherein the bispecific antibody is a single chain Fv heterobispecific dimer.
54. A method promoting the disaggregation of a preformed β -amyloid plaque in the brain of a human, the method comprising:
 - a) providing a bispecific antibody comprising:
 - i) a first antibody binding specificity which confers the ability of the bispecific antibody to cross the blood-brain barrier; and
 - ii) a second antibody specificity conferring the ability of the bispecific antibody to bind to a β -amyloid epitope in a preformed β -amyloid

plaque thereby promoting the disaggregation of the plaque; and

- b) introducing the bispecific antibody of step a) into the circulatory system of the human at a concentration sufficient to result in transcytosis of the bispecific antibody across the blood brain barrier.

- 55. The method of Claim 54 wherein the bispecific antibody is produced by fusing a first and a second hybridoma clone, the first hybridoma clone generating the specificity of step a) i) and the second hybridoma clone generating the specificity of step a) ii).
- 56. The method of Claim 54 wherein the bispecific antibody is produced by recombinant DNA techniques.
- 57. The method of Claim 54 wherein the first and second antibody binding specificities are provided by chemically linking a first antibody, or fragment thereof, to a second antibody, or fragment thereof.
- 58. The method of Claim 57 wherein the first and second antibodies are monoclonal antibodies.
- 59. The method of Claim 57 wherein the bispecific antibody is an $F(ab')_2$ hybrid.
- 60. The method of Claim 56 wherein the bispecific antibody is a single chain Fv heterobispecific dimer.
- 61. A method inhibiting the formation of β -amyloid plaques in the brain of a human, the method comprising:
 - a) providing a bispecific antibody comprising:

- i) a first antibody binding specificity which confers the ability of the bispecific antibody to cross the blood-brain barrier; and
 - ii) a second antibody specificity conferring the ability of the bispecific antibody to bind to a β -amyloid epitope, the second antibody further conferring the ability to catalyze the cleavage of β -amyloid, thereby inhibiting the formation of β -amyloid plaques by reducing levels of free β -amyloid available for incorporation; and
 - b) introducing the bispecific antibody of step a) into the circulatory system of the human at a concentration sufficient to result in transcytosis of the bispecific antibody across the blood brain barrier.
62. The method of Claim 61 wherein the bispecific antibody is produced by fusing a first and a second hybridoma clone, the first hybridoma clone generating the specificity of step a) i) and the second hybridoma clone generating the specificity of step a) ii).
63. The method of Claim 61 wherein the bispecific antibody is produced by recombinant DNA techniques.
64. The method of Claim 61 wherein the first and second antibody binding specificities are provided by chemically linking a first antibody, or fragment thereof, to a second antibody, or fragment thereof.
65. The method of Claim 64 wherein the first and second antibodies are monoclonal antibodies.

66. The method of Claim 64 wherein the bispecific antibody is an $F(ab')_2$ hybrid.
67. The method of Claim 63 wherein the bispecific antibody is a single chain Fv heterobispecific dimer.
68. A therapeutic antibody that specifically binds an epitope contained within positions 10-25 of $A\beta$.
69. A therapeutic antibody that sequesters $A\beta$ peptide from its bound, circulating form in blood, and alters clearance of soluble and bound forms of $A\beta$ in central nervous system and plasma.
70. A therapeutic antibody that sequesters free β -amyloid in the blood and impedes passage of soluble β -amyloid out of the peripheral circulation.
71. A therapeutic antibody that sequesters free β -amyloid in the blood, reduces levels of β -amyloid in the brain of an animal and prevents formation of amyloid plaques in the brain of the animal.
72. The therapeutic antibody of claims 68-71 that is a whole antibody.
73. The therapeutic antibody of claims 68-71 that is a fragment.

75. The therapeutic antibody of claims 68-71 that specifically binds to an epitope having an amino acid between positions 10 and 25 of A β .
75. The therapeutic antibody of claim 68-71 that specifically binds to an epitope having an amino acid between positions 14 and 25 of A β .
76. The therapeutic antibody of claim 68, which specifically binds an epitope contained in positions 14-25 of said A β peptide.
77. The therapeutic antibody of claims 68-71, which is a single chain antibody.
78. An antibody fragment obtained from the therapeutic antibody of any one of claims 68-77.
79. The fragment of claim 78, which is a Fab or F(ab')₂ fragment.
80. The fragment of claim 79, which is an F(ab')₂ fragment.
81. The fragment of claim 79, which is an Fab fragment.
82. The therapeutic antibody or fragment of any one of claims 68-77, wherein the antibody or fragment thereof is produced in a myeloma cell.
83. The therapeutic antibody or fragment of any one of claims 68-82, which, when administered peripherally to a human subject, does not need to cross the subject's

blood-brain barrier to exert its beneficial effects.

84. The therapeutic antibody or fragment of any one of claims 68-82, which, when administered peripherally to a human subject, does not require cellular responses in the subject's brain to exert its beneficial effects.
85. The therapeutic antibody or fragment of any one of claims 68-82, which, when administered peripherally to a human subject, does not substantially bind aggregated A β in the subject's brain.
86. The therapeutic antibody or fragment of any one of claims 68-82, which, when administered peripherally to a human subject, exhibits beneficial effects without necessarily binding to A β plaques in the brain.
87. A nucleic acid, comprising a sequence coding for the light chain or the heavy chain of the antibody of any one of claims 68-86, or a fragment thereof.
88. One or more nucleic acids, which when expressed in a suitable host cell, yield an antibody of any one of claims 68-86.
89. An expression vector for expressing the antibody or fragment of any one of claims 68-86 comprising nucleotide sequences encoding said antibody or fragment.

90. A cell transfected with the expression vector of claim 89.
91. A cell transfected with two expression vectors of claim 89, wherein a first vector comprises a nucleotide sequence encoding a light chain and a second vector comprises a nucleotide sequence encoding a heavy chain.
92. A recombinant cell that produces the therapeutic antibody or fragment of any one of claims 68-82.
93. The cell of any one of claims 90-92, wherein the cell is a myeloma cell.
94. A composition that comprises the antibody or fragment of any one of claims 68-86, and a sterile diluent.
95. A method to inhibit the formation of amyloid plaques or the effects of toxic soluble A β species in humans, which method comprises administering to a human subject in need of such inhibition an effective amount of a therapeutic antibody or fragment thereof that specifically immunoreacts with an epitope contained in positions 10-25 of A β .
96. A method to reduce amyloid plaques or the effects of toxic soluble A β species in humans, which method comprises administering to a human subject in need of such reduction an effective amount of a therapeutic antibody or fragment thereof which specifically immunoreacts with an epitope contained in positions 10-

25 of A β .

97. A method to inhibit the formation of amyloid plaques or the effects of toxic soluble A β species in humans, which method comprises administering to a human subject in need of such inhibition an effective amount of a therapeutic antibody or fragment thereof that sequesters A β peptide from its bound, circulating form in blood.
98. A method to reduce amyloid plaques or the effects of toxic soluble A β species in humans, which method comprises administering to a human subject in need of such reduction an effective amount of a therapeutic antibody or fragment thereof which sequesters A β peptide from its bound, circulating form in blood.
99. The method of any of claims 95-98, wherein said antibody or fragment, when administered peripherally to humans, does not need to cross the blood-brain barrier to inhibit the formation of amyloid plaques or the effects of toxic soluble A β species.
100. The method of any of claims 95-98, wherein said antibody or fragment, when administered peripherally to humans, does not require cellular responses to inhibit the formation of amyloid plaques or the effects of toxic soluble A β species.
101. The method of any of claims 95-98, wherein said antibody or fragment, when administered peripherally to

humans, does not substantially bind aggregated A β in the brain.

102. The method of any one of claims 95-101, wherein the subject has or is at risk for Alzheimer's disease, or Down's syndrome.
103. The method of any one of claims 95-101, wherein the subject is not diagnosed with Alzheimer's disease, or Down's syndrome.
104. The method of any one of claims 95-103, wherein the antibody is administered by a peripheral route.
105. The method of claim 104, wherein the antibody is administered by an intravenous route.
106. A method of treating Alzheimer's disease, comprising administering to a patient in need thereof an effective amount of the antibody or fragment of any one of claims 68-86.